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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/776,190	01/24/1997	HANS-PETER JOSEL	P564-7002	1643

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EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 12/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/776,190	JOSEL ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *72-77,81-89,100 and 107-116* is/are pending in the application.

4a) Of the above claim(s) *82 and 89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72-77,81,83-88,100 and 107-116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/15/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 72-77, 81-89, 100 and 107-116 are pending. Claims 82 and 89 remain withdrawn from consideration as drawn to non-elected species, there currently being no allowable generic claim. Claims 72-77, 81, 83-88, 100 and 107-116 are examined herein to the extent of the elected species.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/15/2005 has been entered.

Election/Restrictions

3. The Requirement for Restriction/Election, mailed 4/27/2000, and applicant's election of Group I, claims 72-89; and applicant's election of the subspecies of (a) amino acids, (B) hormones and (c) luminescent metal chelates; are maintained.

Priority

4. The instant application is the national stage filing under 36 USC 371 of PCT/EP95/02915, filed 7/24/1995. This application claims foreign priority to Germany P 4426276.0, filed 7/25/1994; Germany P 4430998.8, filed 8/31/1994; Germany P 4430973.2, filed 8/31/1994; and Germany P 4439345.8, filed 11/04/1994.

Information Disclosure Statement

5. The Information Disclosure Statement, entered 8/15/2005, has been considered.

Declaration Under 37 CFR 1.132

6. The declaration by Dr. Milan Mrksich, (hereinafter Mrksich Declaration) under 37 CFR 1.132, filed 8/15/2005, is insufficient to overcome the rejection of claims 72-77, 81, 83-88, 100 and 107-116, based upon all pending rejections as set forth in the last Office action, because of the reasons set forth below.

The Declarant at para 11, in discussing the rejection under 35 USC 112, first paragraph, for lack of written description, argues that applicants were in possession of conjugates comprising haptens, markers, or solid phase binding groups coupled to reactive side groups at predetermined position on the polymeric carrier that are incorporated into the carrier at defined and reproducible positions. In discussion of the rejection of the claims under 35 USC 112, second paragraph, at para 15, over the language "predetermined positions", argues that "[t]he Applicants' description of the invention in these functional terms is accurate, efficient and the most informative for

those skilled in the art. Further, a skilled artisan would understand how they could avoid infringing these claims; for example, they could randomly introduce marker groups onto the polypeptide after the peptide synthesis is complete."

Declarant's arguments with regard to the rejection for lack of written description are not persuasive. As stated in the rejection for lack of written description in the previous Office action, the claims provide no notice to the practitioner of structural differences that would result from placement of conjugates at so-called predetermined positions. The claims are drawn to a product that is a conjugate. In comparing a conjugate product made by a process where marker groups were randomly introduced onto the polypeptide, as suggested, with a conjugate made by placing marker groups at "predetermined positions", the examiner respectfully submits that the claimed invention with "predetermined positions" would not be distinguishable from the randomly constructed conjugate. Therefore the claims do not provide a notice function. In that the claimed invention is drawn to a single conjugate, whether or not the groups are at "defined and reproducible positions" would be impossible to assess without knowing the history of the synthesis; i.e., the limitation that placement of the groups occur at "predetermined positions" does not provide a structural limitation to the conjugate product.

In regard to the written description rejection of claim 110, which recites a carrier that is "non-immunologically reactive", Declarant, at para 14, argues that "it is readily apparent to those skilled in the art that the carrier must not interact with antibodies in solution"; and at para 15, points to p. 16 of specification for the disclosure that "peptide

backbone of the conjugate has a non-immunologically reactive amino acid sequence . . . which does not interfere with the test procedure in the *intended application* of the conjugate . . .", (emphasis added).

Declarant's arguments have been considered but are not persuasive. In regard to the requirement that the carrier must not interact with antibodies in solution, Declarant argues limitations not found in the claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

Furthermore, the intended application or use of the claimed product, does not serve to provide a structure or limitation to the conjugate. As the application discloses, whether a carrier is non-immunologically reactive will depend on the specific assay. The examiner does not assume that there are structural features that will produce a non-immunologically reactive carrier (See Declaration at para 17), but rather finds that the term "non-immunologically reactive" does not provide notice to the practitioner of what the claimed carrier is. Furthermore, the examiner respectfully submits that whether a carrier is, or is not "non-immunologically reactive", depends upon what use or application the applicant intends, then the term "non-immunologically reactive" will not provide any structural limitation to claimed product.

For similar reasons, the metes and bound of the claimed conjugates is unclear from the terms "predetermined" and "non-immunologically reactive", which render the claims vague and indefinite under 35 USC 112, second paragraph. The practitioner cannot discern the metes and bounds of a conjugate whose group positions are "predetermined" from a conjugate that whose groups are randomly positioned. The

practitioner cannot discern the metes and bounds of a "non-immunologically reactive" carrier, if the same carrier may or may not be "non-immunologically reactive", depending on what application or use is intended for it.

In regard to the rejection under 35 USC 102 (b) of claims as anticipated by Tam, US 5,229,490, the Declarant states the claims require that the haptens, markers and immobilization groups of the conjugate are bound through an amino or thiol group, but the Tam reference discloses the solid phase as bound to the carrier through a hydroxyl group. Declarant states that the Tam reference does not address the limitations that derive from a non-optimal positioning of haptens, marker groups and immobilization groups on dendritic particles and does not describe any strategies for positioning of the groups.

The statements of the Declarant are considered to be insufficient to overcome the rejection over Tam. Tam does not teach the solid phase as bound to carrier through an amino or thiol group, but the examiner respectfully submits that the Tam reference does teach marker groups of the conjugate bound through an amino group. Because the claims are drawn to conjugating solid phase binding groups or, alternatively, marker groups, a showing that a marker group is bound through an amino or thiol group is sufficient to meet that limitation of the claims. Tam at col. 4, lines 55-68, teach a dendritic polymer base with a plurality of anchoring sites covalently bound to antigenic molecules which may be the same or different, and that the antigenic molecules are not limited to peptide antigens or even antigens. Tam at col. 5, lines 1-10, teach that the selected antigen may be separately synthesized and joined to the carrier or synthesized

on the carrier; and contemplates functional groups on the polymer that are amino groups or carboxyl groups, upon which the antigen can be synthesized. Tam at col. 10, lines 27-40, states that his "multiple antigen peptide system" is not limited to vaccines, but that the core molecules may be used as a carrier and could support a diagnostic agent. Tam at col. 10, lines 40-55, teaches that his multiple antigen peptide system may be employed in various diagnostic tests, including various immunoasssay diagnostic tests. Tam states at col. 10, lines 44-48, "[f]or such testing the diagnostic moiety joined to the dendritic polymer may be labeled with a detectable label, or it may be caused to react with a labeled product such as a labeled antibody to product a detectable reaction product." The examiner respectfully submits that this may be read as "the dendritic polymer . . . may be caused to react with a labeled product . . .". In view of Tam's teaching of the goal of his invention to be a dendritic polymer base with amino functional groups upon which to attach antigens or other molecules, and because Tam teaches that the dendritic polymer "may be caused to react with a labeled product", which includes labels such as fluorescein or rhodamine (Tam at col. 10, lines 48-50), the reference of Tam anticipates the claims.

Furthermore, Declarant allegations in regard to optimal positioning of haptens, marker groups and immobilization groups on dendritic particles and strategies for positioning of the groups, argues for limitations not found in the claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

In regard to the rejection under 35 USC 102(e) of the claims as anticipated by Rose, US 6,001,364, the Declarant states that the claimed invention requires that an oligomeric molecule contain the hapten and either a marker group or immobilization group, all at predetermined positions, whereas the examiner states in the office action, that "the art teaches an amino side group to which is attached a hapten or marker or solid phase binding group." Thus Rose does not teach attaching a hapten and either a marker group or an immobilization group to the oligomer.

The statements of the Declarant are considered to be insufficient to overcome the rejection under 35 USC 102 over Rose. Rose at col. 12, line 45-col. 13, line 8, teaches COSM as organic molecules, which may be an antigen or a hapten (including metal chelates, (col. 6, lines 46-47)). Rose at col. 12, lines 37-45, teach that a baseplate can have at least one baseplate terminal residue attached to a reporter group (such as luciferin) or linker group, typically vial a non-oxime linkage. Rose at col. 13, line 57-col. 14, line 19, teach that a COSM can be a specifically active chelator of metal ions, or used to bind detectable markers. Rose et al. col. 8, lines 37-40, teach that "[e]ach chemoselectively ligated COSM on a baseplate can be independently be the same or different from each other." And again, at col. 7, lines 39-40, Rose teaches that "not all of the COSMs on a single baseplate will be identical." Thus Rose discloses polymer carriers comprising haptens and markers groups coupled to reactive side groups, and so anticipates the rejected claims.

Claim Rejections - 35 USC § 112, First Paragraph

Maintained Claim Rejections

7. Claims 72-77, 81, 83-88, 100 and 107-115 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. This rejection maintains the reason of record as set forth in the previous Office actions.

Applicant, in argument against the instant rejection, refers to the Mrksich Declaration under 37 CFR 1.132, filed 8/15/2005.

Response to Arguments

Applicant's arguments filed 8/15/2002, have been fully considered but they are not persuasive. See, above discussion of the Declaration Under 37 CFR 1.132.

Claim Rejections - 35 USC § 112, Second Paragraph

Maintained Claim Rejections

8. Claims 72-77, 81, 83-88, 100 and 107-115 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is maintained for the reasons of record, as set forth in the previous Office actions.

Applicant, in argument against the instant rejection, refers to the Mrksich Declaration under 37 CFR 1.132, filed 8/15/2005.

Response to Arguments

Applicant's arguments filed 8/15/2002, have been fully considered but they are not persuasive. See, above discussion of the Declaration Under 37 CFR 1.132.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Claim Rejections

9. Claims 72, 74, 75, 81, 85-88, 100, 107, and 110-116 are rejected under 35 U.S.C. 102(b) as being anticipated by Tam (US 5,229,490). This rejection is maintained for the reasons of record, as set forth in the previous Office actions, (mailed 9/16/2004, 2/25/2004, 5/21/2003, 1/16/2002). This rejection is in view of the rejection under 35 USC 112, second paragraph.

In addition to aforementioned reasons of record, Tam, throughout the patent and at col. 10, teaches conjugates that includes steroids, reading on hormone that are steroids, as in claims 112-113. Tam at col. 10, lines 56-65, teach using an immunologically reactive peptide epitope that is viral and derived from HTLV-III virus, reading on HIV I, as in claims 114 and 115) in his conjugate. In regard to newly added claim 116, the reference of Tam teaches using dendritic polylysine wherein the amino groups of lysine are protected (col. 8, lines 9-47) and at col. 3, lines 31-47, teach that an

important feature of the dendritic polymer as an antigen carrier is that the exact structure is known.

Applicant, in argument against the instant rejection, refers to the Mrksich Declaration under 37 CFR 1.132, filed 8/15/2005. Applicant argues again that Tam does not teach or suggest a carrier that simultaneously contains both a hapten molecule and a solid phase binding group. Applicant further argues that Tam does not indicate how to simultaneously introduce hapten, marker groups or immobilization groups at predefined positions that are amino and thiol groups.

Response to Arguments

Applicant's arguments filed 8/15/2002, have been fully considered but they are not persuasive. See, above discussion of the Declaration Under 37 CFR 1.132. Tam does not teach the solid phase as bound to carrier through an amino or thiol group, but the examiner respectfully submits that the Tam reference does teach marker groups of the conjugate bound through an amino group. Because the claims are drawn to conjugating solid phase binding groups or, alternatively, marker groups, a showing that a marker group is bound through an amino or thiol group is sufficient to meet that limitation of the claims.

In regard to applicant's arguments regarding "predefined positions", applicant argues limitation not found in the claims. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., predefined positions) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification,

limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

10. Claims 72, 74-76, 86-88, 100, 107, 110, 111 and 116 are rejected under 35 U.S.C. 102(e) as being anticipated by Rose et al. (US 6,001,364). This rejection is maintained for the reasons of record, as set forth in the previous Office actions, (mailed 9/16/2004, 2/25/2004, 5/21/2003, 1/16/2002). This rejection is in view of the rejection under 35 USC 112, second paragraph.

In addition to aforementioned reasons of record, and in regard to newly added claim 116, Rose et al., throughout the patent, discloses macromolecules of defined structure to which other molecules are attached, (called a baseplate) through a plurality of oxime linkages. Rose et al., at col. 9, lines 22-33, teach making a carrier baseplate may contain an amino-oxy reactive group capable of generating an oxime-linkage.

In the Reply, filed 6/28/2004, to the previous Office action, applicant argues that Rose et al. does not teach or suggest all elements of the claimed invention. Rose does not disclose groups coupled by amino or thiol groups, as in the claims, but rather coupled to oxime groups. Applicant, in argument against the instant rejection, refers to the Mrksich Declaration under 37 CFR 1.132, filed 8/15/2005. Applicant argues again that Rose does not teach attaching a hapten and either a marker group or an immobilization group to the oligomer.

Response to Arguments

Applicant's arguments filed 6/28/2004, have been fully considered but they are not persuasive. As stated in the Response to Arguments for the rejection under 35 U.S.C. 102(b) over Rose et al., the reference of Rose teaches and suggests hapten molecules and marker groups or solid phase binding groups that are coupled to a polymeric carrier by reactive amino groups. The examiner respectfully notes that the Mrksich Declaration is silent on this limitation of the claims.

Rose et al., at col.s 1-2, "Introduction", teach two methods have traditionally been used to produce complex polymers, such as polypeptides. One method relies on relatively uncontrolled polymerization reactions to produce large polymers such as polypeptides and plastics . Rose states that "[w]hile such polydisperse macromolecules can be relatively easy to produce, the polymeric macroscopic products are not homogeneous at the molecular level but are mixtures of polymers of different lengths and even different composition, e.g., in a random copolymer). Furthermore, the similarity of the homologs produced in such polydisperse preparations makes it difficult or impossible to obtain a single high molecular weight product in pure form."

Rose et al. teach that a second method has been the sequential assembly of reversibly protected monomers of defined, typically linear, structure. Rose teaches that this method is limited in the size and, most critically, the complexity of molecules that can be produced; for example, synthesis of defined polypeptides or proteins larger than about 50-80 amino acid residues has been beyond the reach of this technology. Condensation of pre-purified protected peptides, two at a time, is limited by the

insolubility of large protected fragments. As a result, synthesis of homogeneous, linear polypeptides, for example, is limited to an upper limit of about 100 amino acid residues. In reviewing the background of this method, Rose states:

> Mutter et al. (Proteins: Structure, Function and Genetics (1989) 5: 13-21) have synthesized branched chain polypeptides by step-wise coupling of protected amino acids to a synthetic, protected, resin-bound peptide template during solid-phase peptide synthesis. Deprotection and cleavage was required to obtain a soluble template-assembled synthetic protein. Also using step-wise, solid phase peptide synthesis, Tam and Zavala (J. Immunol. Meth. (1989) 124: 52-61) have built branched chain "lysine tree" templates with peptide branches, referred to as multiple antigen peptides, which were subsequently obtained in soluble, crude form after HF deprotection and cleavage.

Rose et al., at col. 1, lines 49-60. Rose notes that the protecting groups used in polypeptide synthesis decreases solubility, but that the use of unprotected precursors raises problems of regiospecificity.

To overcome this problem of regiospecificity, workers have employed chemoselective ligation, which uses complementary pairs of reactive groups present at specific sites on the precursor molecules to be joined (col. 2, lines 5-20). Thiol groups and bromoacetyl groups have been used as the reactive groups, and result in regiospecific bonds. Rose et al., at col. 2, lines 20-13, states: "thiol-type chemoselective ligations have been used to prepare a multi-antigenic peptides." Rose states:

> In an attempt to avoid harsh deprotection methods and formation of impure products caused by possible steric hindrance between closely spaced growing peptide arms during step-wise solid phase synthesis, Drijfhout and Bloemhoff (Int. J. Peptide Protein Res. (1991) 37: 27-32) used thiol-type chemoselective coupling by synthesizing a branched "octa-lysine tree" peptide, whose deprotected epsilon amino groups were extended to contain protected sulfhydryl groups (S-acetylmercaptoacetyl)

> for subsequent coupling to an appropriately modified sulfhydryl-containing antigenic peptide.

Rose at col. 2, lines 13-23.

Rose, at col. 2, lines 29-37, teaches that this thiol chemistry is not completely specific. In order to address these problems, Rose et al. discloses macromolecules of defined structure to which other molecules are attached, (called a baseplate) through a plurality of oxime linkages. Rose at col. 2-3, teach baseplates having a plurality of oxime-forming reactive groups and a second organic molecules, referred to as a complementary orthogonal specifically active molecule (COSM) that has an orthogonal reactive group complementary in oxime linkage. Rose at col. 9, lines 22-33, teach that the baseplate may contain as one complementary reactive group capable of oxime-linkage that is an amino-oxy group, including amino-oxy-acetyl (AOA) groups. Rose states:

> A "lysine tree" formed by solid phase peptide synthesis as illustrated by Tam and Zavala (J. Immunol. Meth. (1989) 124: 52-61), which is incorporated herein by reference, is suitable for use in template formation if modified as described herein to contain oxime-forming complementary orthogonal reactive groups of the same orientation. . . . When the baseplate is formed from amino acids, the peptide sequence of a baseplate structure can be synthesized by routine solid phase peptide synthesis ("SPPS") and, while the peptide is still attached to the solid phase, Boc-amino-oxyacetic acid (Boc-AOA) in an activated form such as the N-hydroxysuccinimide ester can be added to the nascent peptide chain. For example, the baseplate structure can consist of a peptide having five reactive groups such as five lysine residues. Boc-AOA N-hydroxysuccinimide ester can react with each of the .epsilon.-amino groups of the lysine residues, as well as the N-terminus .alpha.-amino group if left unprotected, to form the baseplate structure which, in this example, would contain an .epsilon.-AOA-pentalysine sequence and an AOA group at the N-terminus, if the N-terminus .alpha.-amino group was intentionally acylated.

Rose et al. at col. 10, line 56-col. 11, line 22.

Therefore, the examiner respectfully submits that the reference of Rose discloses groups, which are coupled to reactive side groups, wherein the reactive side group are amino and groups and/or thiol groups, particularly amino-oxy groups.

Rose at col. 12, line 45-col. 13, line 8, teaches COSM as organic molecules, which may be an antigen or a hapten (including metal chelates, (Rose at col. 6, lines 46-47). Rose at col. 12, lines 37-45, teach that a baseplate can have at least one baseplate terminal residue attached to a reporter group (such as luciferin) or linker group, typically vial a non-oxime linkage. Rose at col. 13, line 57-col. 14, line 19, teach that a COSM can be a specifically active chelator of metal ions, or used to bind detectable markers. Rose et al. col. 8, lines 37-40, teach that "[e]ach chemoselectively ligated COSM on a baseplate can be independently be the same or different from each other." And again, at col. 7, lines 39-40, Rose teaches that "not all of the COSMs on a single baseplate will be identical." Thus Rose disclose polymer carriers comprising haptens and markers groups coupled to reactive side groups, as in the instant claims.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Claim Rejections

11. Claims 72, 74-77, 81, 85-88, 100, 107-116 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Tam (US 5,229,490). This rejection is maintained for the reasons of record, as set forth in the previous Office actions, (mailed 9/16/2004, 2/25/2004, 5/21/2003, 1/16/2002).

In addition to aforementioned reasons of record, Tam, throughout the patent and at col. 10, teaches conjugates that includes steroids, reading on hormone that are steroids, as in claims 112-113. Tam at col. 10, lines 56-65, teach suing an immunologically reactive peptide epitope that is viral and derived from HTLV-III virus, reading on HIV I, as in claims 114 and 115). In regard to newly added claim 116, the reference of Tam et al., teaches using dendritic polylysine wherein the amino groups of lysine are protected (col. 8, lines 9-47) and at col. 3, lines 31-47, and teach that an important feature of the dendritic polymer as an antigen carrier is that the exact structure is known. It would have been obvious to make conjugates containing 1-6 hapten molecules (as in claim 76) and to make conjugates having 2-8 marker groups (as in claim 77) because Tam teaches making conjugates with haptens and marker groups.

Applicant, in argument against the instant rejection, refers to the Mrksich Declaration under 37 CFR 1.132, filed 8/15/2005. Applicant argues again that Tam does not teach or suggest a carrier that simultaneously contains both a hapten molecule and a solid phase binding group. Applicant further argues that Tam does not indicate

how to simultaneously introduce hapten, marker groups or immobilization groups at predefined positions that are amino and thiol groups.

Response to Arguments

Applicant's arguments filed 8/15/2002, have been fully considered but they are not persuasive, (see above rejection under 35 USC 102(b)).

12. Claims 72-76, 81, 83-88, 100, 107-111 and 116 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al. (US 6,001,364). This rejection is maintained for the reasons of record, as set forth in the previous Office actions.

In addition to aforementioned reasons of record, and in regard to newly added claim 116, Rose et al., throughout the patent, discloses macromolecules of defined structure to which other molecules are attached, (called a baseplate) through a plurality of oxime linkages and, at col. 9, lines 22-33, teach making a carrier baseplate may contain an amino-oxy reactive group capable of oxime-linkage. Rose at col. 13, line 57-col. 14, line 19, teach that a COSM can be a specifically active chelator of metal ions, or used to bind detectable markers, wherein the detectable markers include luciferase. Rose at col. 16, line 40-col. 17, line 8, teaches COSM that are metal chelating agents, and chelating or reporter agents that are coupled to the baseplate. Rose at col. 28, lines 39-44, teach multimers having varying spacing, charge, and other desirable physical and biological properties. Therefore, it would have been obvious to make luminescent metal chelates and polymeric carriers containing negatively or positively charged groups (as in claims 73, 83, 84).

In the Reply, filed 6/28/2004, to the previous Office action, applicant argues that Rose et al. does not teach or suggest all elements of the claimed invention. Rose does not disclose groups coupled by amino or thiol groups, as in the claims, but rather coupled to oxime groups. Applicant, in argument against the instant rejection, refers to the Mrksich Declaration under 37 CFR 1.132, filed 8/15/2005. Applicant argues again that Rose does not teach attaching a hapten and either a marker group or an immobilization group to the oligomer.

Response to Arguments

Applicant's arguments filed 6/28/2004, have been fully considered but they are not persuasive, (see above rejection under 35 USC 102(e)).

Conclusion

13. Claims 72-77, 81, 83-88, 100 and 107-116 are rejected. Claims 82 and 89 remain withdrawn from consideration.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

ms

PADMASHRI PONNALURI
PRIMARY EXAMINER